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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/733,855

12/10/2003

Peter A. Carr

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EXAMINER

LU, FRANK WEI MIN

ART UNIT

PAPER NUMBER

1634

MAIL DATE

DELIVERY MODE

08/19/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/733,855	Applicant(s) CARR ET AL.	
	Examiner FRANK W. LU	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 5/19/2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 1-3 and 6-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4,5 and 11-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 September 2004 and 30 August 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE and the amendments filed on May 19, 2008 have been entered. The claims pending in this application are claims 1-18 wherein claims 1-3 and 6-10 have been withdrawn due to restriction requirements mailed on June 2, 2006. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of applicant's amendment filed on May 19, 2008. Claims 4, 5, and 11-18 will be examined.

Claim Objections

2. Claim 4 is objected to because of the following informality: "nucleic acid" in step b) should be "a nucleic acid" or "nucleic acids".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. New Matter

Claims 12, 13, 15, and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 12 or claim 15 contains a limitation “detecting change in electrophoretic force exerted by the synthesized growing nucleic acid on the solid support as it grows”. Since the paragraphs [0022] and [0119] of US 2005/0227235 A1 (US publication of this instant application) suggested by applicant fail to define or provide any disclosure to support such claim limitation, this limitation is considered as a new matter. Furthermore, although paragraphs [0026], [0027] and [0125]-[0130], and [0135] of the specification, Figures 11A, 11B, 12 A and 12B, and original filed claim 7 suggested by applicant describe that parallel single-molecule systems may use arrays of light sources and detectors and describe the parallelization of single-molecule systems with and without arrays of light sources and detectors, since paragraphs [0026], [0027] and [0125]-[0130], and [0135] of the specification, Figures 11A, 11B, 12 A and 12B, and original filed claim 7 do not describe a limitation “a plurality of reactions comprising steps (a)- (e) are carried out in parallel using a plurality of light sources and detectors” as recited in claims 13 and 16, this limitation is also considered as a new matter.

MPEP 2163.06 notes “IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).” MPEP 2163.02 teaches that “Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject

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matter is not described in that application.” MPEP 2163.06 further notes “WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT “NEW MATTER” IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*” (emphasis added).

Response to Arguments

In page 7, last paragraph bridging to page 8, first paragraph of applicant’s remarks, applicant argues “the limitation of claims 12 and 15 is clearly disclosed in paragraphs [0022] and [0119] of the Specification, which state, in part: ‘The support is held in a fixed equilibrium position by applying an electric field and magnetic field gradient created by the magnetic tweezers that opposes the electrophoretic force Assuming the zeta-potential of the dielectric bead is constant, *the addition of an oligonucleotide strand is the only contribution to the increase in electrophoretic force felt by the particle.* The increased electrophoretic force moves the bead from its equilibrium position, and the magnetic field gradient must be increased to restore the bead to its equilibrium position. *Optically determined bead velocity and restoration force correspond to the number of bases added.* Therefore, the length of the added strand can be ensured to be correct.’ (emphasis added). A suitable apparatus is depicted in Figs. 15F and G, and described in paragraph [0143], while the results from an actual experimental run of a reduction to practice of the methodology claimed is depicted in Figs. 15A-E and described in paragraphs [0137] [0142]. The Applicants therefore respectfully maintain that the limitation of claims 12 and 15 is fully supported by the written description, that it is clear that the inventors, at the time the application was filed, had possession of the claimed invention, that the underlying technology of the limitation is well-known in the art of the invention, and that the rejected claims therefore satisfy the requirements of 35 U.S.C. 112, first paragraph”.

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These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, paragraphs [0022] and [0119] of the specification mentioned by applicant appear to be paragraphs [0022] and [0119] of US 2005/0227235 A1, which is US publication of this instant application, and does not appear to be paragraphs [0022] and [0119] of the specification. Second, although paragraphs [0022] and [0119] of US 2005/0227235 A1 suggested by applicant describes that “the addition of an oligonucleotide strand is the only contribution to the increase in electrophoretic force felt by the particle” and “[O]ptically determined bead velocity and restoration force correspond to the number of bases added”, paragraphs [0022] and [0119] of US 2005/0227235 A1 do not describe “detecting change in electrophoretic force exerted by the synthesized growing nucleic acid on the support as it grows” as recited in claims 12 and 15 because claims 12 and 15 do not limit the support as a particle or bead.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 4, 5, and 11-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 4 is rejected as vague and indefinite because it is unclear whether “errors” in step d) is identical to “errors” in step e) or not. If “errors” in step d) is identical to “errors” in step e), “errors” in step e) should be “the errors”. Please clarify.

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8. Claim 5 is rejected as vague and indefinite. Since the claim does not indicate that the sequence of the synthesized nucleic acid has deletion errors in the sequence and how the deletion errors in the sequence of the synthesized nucleic acid is correlated with the deprotection of the 5' protecting group, it is unclear why the deletion errors in the sequence of the synthesized nucleic acid can be eliminated by the step of monitoring the deprotection of the 5' protecting group as recited in step b). Please clarify.

9. Claim 11 is rejected as vague and indefinite. Since the claim does not indicate that the composition of a deprotection wash, it is unclear why the deprotection wash can deprotect the synthesized nucleic acid. Please clarify.

10. Claim 12 or 15 is rejected as vague and indefinite. Since the claim does not indicate how electrophoretic force is correlated with synthesized growing nucleic acid on the solid support as it grows, it is unclear why change in electrophoretic force can be exerted by the synthesized growing nucleic acid on the solid support as it grows. Please clarify.

Response to Arguments

In page 9, last paragraph bridging to page 10, first paragraph of applicant's remarks, applicant argues "[A]s discussed in the previous section, and disclosed in the Specification, the embodiment claimed in claim 12 makes use of a magnetic (or optical) tweezer. The addition of an oligonucleotide strand creates an increase in electrophoretic force felt by the support, as is well known, which increased electrophoretic force moves the support from its equilibrium position and necessitates increasing the magnetic field gradient in order to restore the support to the equilibrium position. The restoration force may then be used to determine the number of

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bases added. The Applicants therefore respectfully submit that the limitation of claim 12 is neither vague nor indefinite, being fully disclosed and supported in the Specification”.

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. Since the claim does not indicate how electrophoretic force is correlated with synthesized growing nucleic acid on the solid support as it grows, it is unclear why change in electrophoretic force can be exerted by the newly synthesized growing nucleic acid on the solid support as it grows.

11. Claim 14 is rejected as vague and indefinite. Since claim 4 does not indicate that the sequence of the synthesized nucleic acid has at least one 5' protecting group and has deletion errors in the sequence, and how the deletion errors in the sequence of the synthesized nucleic acid is correlated with the deprotection of the 5' protecting group, it is unclear why deletion errors in the sequence of the synthesized nucleic acid can be eliminated by the step of monitoring the deprotection of the 5' protecting group as recited in claim 14. Please clarify.

12. Claim 18 is rejected as vague and indefinite. Since claim 5 only describes deletion errors while the errors in the sequence of the synthesized nucleic acid of claim 18 are selected from the group consisting of insertion errors, deletion errors, and wrong base incorporation errors, claims 5 and 18 do not correspond each other. Please clarify.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 4 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Gascoyne *et al.*, (US 2003/0171325, priority date: January 4, 2002).

Regarding claim 4, Gascoyne *et al.*, teach providing a solid support for synthesis of nucleic acid, synthesizing nucleic acid attached to the solid support (ie., the beads) (see pages 3 and 4, and [0033] to [0038]), passing the solid support and synthesized nucleic acid through a channel opening (ie., transporting the beads attached synthesized oligos into top right of the center channel wherein the center channel is a channel with an opening, see page 4, [0039] and [0040] and page 13, [0152] and Figure 1), detecting errors in the sequence of the synthesized nucleic acid, and correcting errors in the sequence of the synthesized nucleic acid (see pages 4-7, and [0048] to [0079]).

Regarding claim 17, Gascoyne *et al.*, teach that the errors in the sequence of the synthesized nucleic acid are selected from the group consisting of insertion errors, deletion errors, and wrong base incorporation errors (see page 1, [0013] and [0014]).

Therefore, Gascoyne *et al.*, teach all limitations recited in claims 4 and 17.

Response to Arguments

In page 10, last paragraph bridging to page 11, second paragraph of applicant's remarks, applicant argues that: (1) "[T]he Applicants respectfully traverse the rejections, on the grounds that any rejection over Gascoyne is improper, because the filing date of Gascoyne is too late for Gascoyne to be available for use as prior art against the present application. The filing date of the Gascoyne application is January 3, 2003. The instant application was filed December 10, 2003

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and claims the benefit under 35 U.S.C. 119(e) of U.S. Prov. App. Ser. No. 60/432,556 ('the '556 provisional'), filed December 10, 2002. The Applicants respectfully note that the Applicants' claim for the benefit of the '556 provisional is reflected in the Application Data presented on the USPTO website and that the Applicants' Specification contains the required language referring to the earlier application"; and (2) "[T]he prior art provisions of 35 U.S.C. 102(e), as laid out in the Office Action, require that the invention be described in a an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent. By virtue of the claim for benefit to the '556 provisional application, which was filed on December 10, 2002, the effective cutoff filing date for the availability of a published application for use as prior art against the present application is therefore December 9, 2002 (the 'critical date'). The filing date of Gascoyne, January 3, 2003, is after the critical date of December 9, 2002. The Gascoyne reference is therefore not available for use as prior art against the present application".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. Although the filing date of the US publication from Gascoyne *et al.*, was January 3, 2003, since the priority date of this US publication was January 4, 2002, the US publication from Gascoyne *et al.*, can be used as a prior art against this instant application which has the priority date of December 9, 2002.

Conclusion

15. No claim is allowed.

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16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Frank W Lu /
Primary Examiner, Art Unit 1634
August 18, 2008

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	10/733,855	CARR ET AL.	
	Examiner	Art Unit	
	FRANK W. LU	1634	